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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,930	10/16/2001	Jacques Delarge	P66806US0	9910

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 03/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/868,930	DELARGE et al.
Examiner	**Art Unit**
Brenda Coleman	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 12-22 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 12-22 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 12-22 are pending in the application.

Priority

1. Any non-provisional application claiming the benefit of one or more prior filed copending nonprovisional applications or international applications designating the United States of America must contain or be amended to contain in the first sentence of the specification following the title a reference to each such prior application, identifying it by application number (consisting of the series code and serial number) or international application number and international filing date and indicating the relationship of the applications. Cross - references to other related applications may be made when appropriate.

"This application is a national stage entry under 35 U.S.C. § 371 of PCT/EP00/00225, filed January 12, 2000." is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 12, 13, 18 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention. The definition of R_1 and/or R_2 form with Y_1 and/or Y_2 a 5 to 7 membered heterocyclic group, saturated or unsaturated. There is no definition in the specification for the heterocyclic groups as claimed herein. The heterocyclic moiety which is defined for the substituents R_1 and/or R_2 form with Y_1 and/or Y_2 in the claims is opened ended and reads on all such rings and ring systems of which are neither supported nor contemplated. *In re Lund 153 USPQ 625.*

3. Claims 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the composition and method claims are not adequately enabled solely based on its inhibitory effect on thromboxan A2 provided in the specification. Instant claim language embraces disorders not only for treatment but for **prevention** which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop myocardial infarction, myocardial ischemia, pulmonary hypertension, etc. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 12-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 12-22 are vague and indefinite in that it is not known what is meant by "derivates".

b) Claim 12 (and claims dependent thereon) recites benzene-sulphonamide derivates have the **general** formula (I). A formula is not general when all of the variables are defined. Deletion of "general" is suggested.

c) Claim 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of X where X is a nitro, cyano, halogen group, **eventually radioactive**.

d) Claim 12 (and claims dependent thereon) are vague and indefinite in that the definition of X is not stated as a proper Markush group.

e) Claim 12 (and claims dependent thereon) are vague and indefinite in that the definition of X ends with a period indicating the end of the claim which is not so.

f) Claim 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of Y_2, which is a divalent variable, however, the definition of Y_2 is to monovalent moieties, i.e. -NH or nitrogen.

g) Claim 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of Y_2 where Y_2 is nitrogen. What else is bonded to the nitrogen atom?

h) Claim 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by a **ramified** alkyl.

i) Claim 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of R_1 and R_2 where R_1 and R_2 are **eventually radioactive**.

j) Claims 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of R_1 and R_2 where R_1 and R_2 are substituted or not by one or several **alkyl groups in C_1-C_4**.

k) "Derivatives" in the proviso of claim 12 (and claims dependent thereon) implies more then what is positively recited. "Compound" is suggested.

l) Claims 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of X in the proviso which is followed by a comma and a period indicating the end of the claim which is not so.

m) Claims 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of R_2 in the proviso which is followed by a comma.

n) Claims 12 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by the definition of R_1 in the proviso, where R_1 is "an element selected in a group constituted".

o) Claim 12 recites the limitation "m-toluyl" in the definition of R_1 in the proviso. There is insufficient antecedent basis for this limitation in the claim.

p) Claim 13 is vague and indefinite in that the definition of X is not stated as a proper Markush group.

q) Claim 14 is vague and indefinite in that it is not known what is meant by the definition of Y_1, which is a divalent variable, however, the definition of Y_1 is to monovalent moiety, i.e. -NH.

r) Claim 14 recites the limitation "oxygen" in the definition of Y_2. There is insufficient antecedent basis for this limitation in the claim.

s) Claim 15 recites the limitation "m-toluyl, o-toluyl and p-toluyl" in the definition of R_1 and R_2. There is insufficient antecedent basis for this limitation in the claim.

t) Claim 15 recites the limitation "caproyl" in the definition of R_1 and R_2. There is insufficient antecedent basis for this limitation in the claim.

u) Claim 15 is vague and indefinite in that it is not known what is meant by the moiety 1-phenylthyl in the definition of R_1 and R_2.

v) Claim 16 is vague and indefinite in that it is not known what is meant by the moiety homopiperidin. It is believed that the applicants intended homopiperidinyl.

w) Claim 17 is vague and indefinite in that it is not known what is meant by the moiety morpholin or homopiperidin. It is believed that the applicants intended morpholinyl or homopiperidinyl.

x) Claim 18 is vague and indefinite in that it is not known what is meant by characterized in that **it is constituted by a salt chosen into the group**.

y) Claim 18 is vague and indefinite in that it is not known what is meant by a potassic salt.

z) Regarding claim 18, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

aa) Claim 19 recites the limitation "metatoluyl" in the second species. There is insufficient antecedent basis for this limitation in the claim.

ab) Claim 19 recites the limitation "cyclohexen-2-yl" in the fourth species. There is insufficient antecedent basis for this limitation in the claim.

ac) Claim 19 is vague and indefinite in that the fourth species is missing an open parenthesis in the nomenclature.

ad) Claim 20 is vague and indefinite in that it is not known what is meant by **eventually other therapeutic agents**.

ae) Claims 21 and 22 provide for the use of the compounds of formula (I), but, since the claim does not set forth any steps involved in the method/process, it is unclear

what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

af) Regarding claim 21, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

ag) Claims 21 and 22 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by inhibiting the activity of thromboxan A2. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties *in vitro*, when administered to a patient with a certain disease, does not produce a favorable response. One can not conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration can not be predicted in advance. Should our drug be given as a bolus *iv* or in a time release *po* formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active *in vitro*, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of whom are inhibitors *in vitro*, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the

accurate answer, and that the success of second compound arises from some other unknown property which the second drug is capable. It is common for a drug, particularly in platelet aggregation, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to effect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 21 and 22 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

5. Claims 12, 18 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Muller et al., U.S. 6,525,211. Muller teaches the compounds and compositions of the instant invention where Y_1-R_1 is OPr-n, OMe, etc. and Y_2-R_2 is 4-methyl-3-(methylthio)-5-oxo-1H-1,2,4-triazole,

4-methyl-3-(ethoxy)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-(ethyl)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-(methoxy)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-(isopropoxy)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-(ethylthio)-5-oxo-1H-1,2,4-triazole, etc. See examples 169, 170, 171, 360-368, etc.

6. Claims 12, 13, 17, 18 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Muller et al., U.S. 6,525,211. Muller teaches the compounds and compositions of the instant invention where Y_1-R_1 is pyrrolidinyl, morpholinyl, NEt_2, NHPr-n, etc. and Y_2-R_2 is 4-methyl-3-(ethoxy)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-(methylthio)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-(ethyl)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-(ethylthio)-5-oxo-1H-1,2,4-triazole, 4-methyl-3-propyl-5-oxo-1H-1,2,4-triazole, 4-methyl-3-methyl-5-oxo-1H-1,2,4-triazole, etc. See examples 169, 170, 171, 360-368, etc. See examples 15-20, 24, 27-34, 39, etc.

7. Claims 12, 15 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Schlebe et al., Journal fuer Praktische Chemie. Schlebe teaches the compounds of the instant invention where Y_1-R_1 is OMe and Y_2-R_2 is -NHPh or -NH-CH_2-CH=CH_2. See examples 5 and 8.

8. Claims 12-14, 18 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Wittner et al., Pfluegers Archiv. Wittner teaches the compounds and compositions of the instant invention where Y_1-R_1 is 3-methylphenylamino and Y_2-R_2 is -NHPr-i. See example 35.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner

can normally be reached on Mondays from 8:30 AM to 5:00 PM, on Tuesdays from 8:00 AM to 4:30 PM, on Wednesday thru Friday from 9:00 AM to 5:30 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brenda Coleman

Brenda Coleman
Primary Examiner AU 1624
March 28, 2003